

Supplementary materials for

Boon HA, Van den Bruel A, Struyf T, Gillemot A, Bullens D, Verbakel JY. Clinical features for the diagnosis of pediatric urinary tract infections: systematic review and meta-analysis. *Ann Fam Med.* 2021;19(5):437-446.

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The supplementary material had been provided by the authors to give readers additional information about their work.

Appendix 1. PRISMA – DTA (diagnostic test accuracy) checklist

	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	4
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	5-6
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6

METHODS			
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	6
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	6-7

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	7-8
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	8
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	8-10
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	8-10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	10

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	10-11
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	12-13
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	13

Adapted From: McInnes MDF, Moher D, Thoms BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163. For more information, visit: www.prisma-statement.org.

Appendix 2. Electronic search strategy (PubMed/MEDLINE)

Concept 1: Urinary tract infections (bladder, kidney)

"Urinary Tract Infections"[Mesh] OR "Infection/urine"[Mesh] OR "cystitis"[Mesh] OR "pyelitis"[Mesh] OR "Pyonephrosis"[Mesh] OR "Pyelonephritis"[Mesh] OR "Urethritis"[Mesh] OR urinary-tract-infection*[tiab] OR UTI[tiab] OR ((infection*[tiab] OR inflam*[tiab]) AND (bladder[tiab] OR kidney[tiab] OR "urinary tract"[tiab])) OR bacteriuria*[tiab] OR pyuria*[tiab] OR bladder-infection*[tiab] OR "bladder inflammation"[tiab] OR cystitis[tiab] OR cystitides[tiab] OR urethritis[tiab] OR pyelocystitis[tiab] OR cystopyelitis[tiab] OR kidney-infection*[tiab] OR pyelitis[tiab] OR pyelonephritis[tiab] OR pyelonephritides[tiab] OR urosepsis[tiab] OR pyonephrosis[tiab]

Concept 2: Signs and symptoms, diagnostic tests, clinical prediction rules

"Signs and Symptoms"[Mesh] OR "Diagnostic Techniques and Procedures"[Mesh] OR "Diagnosis"[Mesh:NoExp] OR "Clinical Decision-Making"[Mesh] OR "Decision Support Techniques"[Mesh] OR "Decision Trees"[Mesh] OR "diagnosis"[Subheading] OR "Reagent Kits, Diagnostic"[Mesh] OR "Point-of-Care Systems"[Mesh] OR "Biomarkers"[Mesh] OR "C-Reactive Protein"[Mesh] OR "Lactic Acid"[Mesh] OR "Procalcitonin"[Mesh] OR "Nitrates/urine"[Mesh] OR "leukocyte esterase" [Supplementary Concept] OR "Peroxidase/urine"[Mesh] OR "Lactoferrin/urine"[Mesh] OR "Immunoglobulin A, Secretory/urine"[Mesh] OR diagnos*[tiab] OR sign[tiab] OR signs[tiab] OR symptom*[tiab] OR clinical-feature*[tiab] OR clinical-assessment[tiab] OR anamnesis[tiab] OR "medical history"[tiab] OR symptom-evaluation*[tiab] OR symptom-assessment*[tiab] OR physical-examination*[tiab] OR clinical-examination*[tiab] OR clinical-impression*[tiab] OR intuition[tiab] OR "gut feeling"[tiab] OR prediction-rule*[tiab] OR decision-tree*[tiab] OR decision-support-techni*[tiab] OR decision-model*[tiab] OR decision-support-model*[tiab] OR appgar-score*[tiab] OR visual-analogue-scale*[tiab] OR "generally unwell"[tiab] OR lethargy[tiab] OR consciousness[tiab] OR confusion[tiab] OR disorientation[tiab] OR convulsion*[tiab] OR irritability[tiab] OR edema[tiab] OR deshydration[tiab] OR jaundice[tiab] OR pallor[tiab] OR sleepiness[tiab] OR capillary-refill-time*[tiab] OR vital-sign*[tiab] OR parameter*[tiab] OR saturation*[tiab] OR heart-rate*[tiab] OR pulse*[tiab] OR blood-pressure*[tiab] OR body-temperature*[tiab] OR fever[tiab] OR pyrexia[tiab] OR shivering[tiab] OR chills[tiab] OR hypotherm*[tiab] OR respiratory-rate*[tiab] OR dyspnea[tiab] OR hypoxia[tiab] OR tachypnea[tiab] OR cyanosis[tiab] OR "failure to thrive"[tiab] OR failure-to-thrive[tiab] OR weight[tiab] OR feeding[tiab] OR "fluid intake"[tiab] OR constipation[tiab] OR diarrhea[tiab] OR nausea[tiab] OR vomiting[tiab] OR "urine appearance"[tiab] OR oliguria[tiab] OR polyuria[tiab] OR dysuria[tiab] OR mictalgia[tiab] OR "malodorous urine"[tiab] OR "cloudy urine"[tiab] OR "smelly urine"[tiab] OR incontinence[tiab] OR stranguria[tiab] OR frequency[tiab] OR urgency[tiab] OR haematuria[tiab] OR hematuria[tiab] OR "flank pain"[tiab] OR "back pain"[tiab] OR "suprapubic pain"[tiab] OR "suprapubic discomfort"[tiab] OR "abdominal pain"[tiab] OR "abdominal tenderness"[tiab] OR "costovertebral angle pain"[tiab] OR "costovertebral angle tenderness"[tiab] OR palpation[tiab] OR "painful kidney"[tiab] OR "palpable kidney"[tiab] OR percussion[tiab] OR uncircumcis*[tiab] OR "dysplastic kidney"[tiab] OR "Vesico-Ureteral Reflux"[tiab] OR laboratory-technique*[tiab] OR laboratory-test*[tiab] OR lab-test*[tiab] OR hematology-test*[tiab] OR hematological-test*[tiab] OR hematologic-test*[tiab] OR blood-test*[tiab] OR blood-gas*[tiab] OR point-of-care-test*[tiab] OR point-of-care-system*[tiab] OR POC-test*[tiab] OR POCT[tiab] OR near-patient-test*[tiab] OR rapid-test*[tiab] OR point-of-care-techn*[tiab] OR bedside-test*[tiab] OR biomarker*[tiab] OR marker*[tiab] OR biochemical-marker*[tiab] OR immunologic-test*[tiab] OR immunological-test*[tiab] OR "CRP"[tiab] OR "c reactive protein"[tiab] OR "c-reactive protein"[tiab] OR procalcitonin[tiab] OR nitrate[tiab] OR leucocyte[tiab] OR "erythrocyte sedimentation"[tiab] OR "glomerular filtration"[tiab] OR GFR[tiab] OR urea[tiab] OR lactoferrin[tiab] OR antimicrobial-peptide*[tiab] OR myeloperoxidase[tiab] OR interleukin*[tiab] OR "xanthine oxidase"[tiab] OR heparin-binding-protein*[tiab] OR "secretory IgA"[tiab] OR proteinase-inhibitor*[tiab] OR electrolyte*[tiab] OR "full blood count"[tiab] OR FBC[tiab] OR "lactic acid"[tiab] OR LDH[tiab] OR lactate[tiab] OR urine-test*[tiab] OR urinalysis[tiab] OR cytology[tiab] OR kidney-function-test*[tiab] OR urine-culture*[tiab] OR reagent-strip*[tiab] OR dipstick[tiab] OR test-strip*[tiab]

Concept 3: Children 0-18y

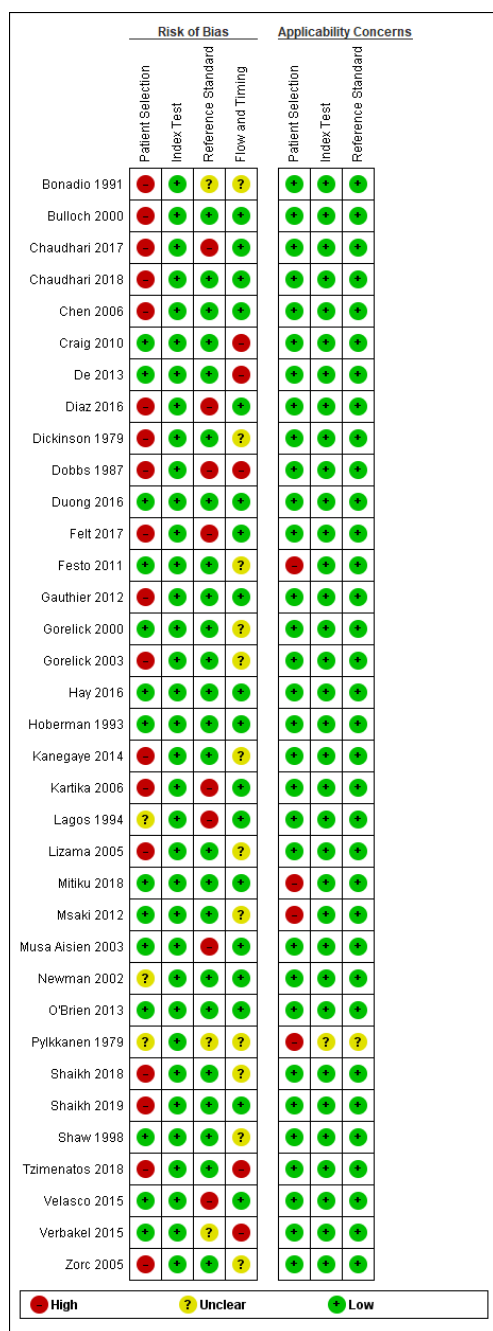
"Child"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR "Minors"[Mesh] OR baby[tiab] OR babies[tiab] OR newborn*[tiab] OR neonat*[tiab] OR perinatal*[tiab] OR postnatal*[tiab] OR post-

natal*[tiab] OR premature*[tiab] OR preterm*[tiab] OR pre-term*[tiab] OR child*[tiab] OR schoolchild*[tiab] OR pediatric*[tiab] OR paediatric*[tiab] OR toddler*[tiab] OR infant*[tiab] OR infancy[tiab] OR preteen*[tiab] OR pre-teen*[tiab] OR prepubertal*[tiab] OR prepubescent*[tiab] OR pubescent*[tiab] OR puberty[tiab] OR preschool*[tiab] OR pre-school*[tiab] OR boy*[tiab] OR girl*[tiab] OR minor*[tiab] OR kid[tiab] OR kids[tiab] OR offspring[tiab] OR adolescen*[tiab] OR teens[tiab] OR teenager*[tiab] OR youth*[tiab] OR student*[tiab] OR underage*[tiab] OR juvenile*[tiab] OR junior*[tiab] OR puerile*[tiab] OR young*[tiab] OR "day old"[tiab] OR "days old"[tiab] OR "month old"[tiab] OR "months old"[tiab] OR "age 1"[tiab] OR "age one"[tiab] OR "ages 1"[tiab] OR "ages one" OR 1-year-old*[tiab] OR one-year-old*[tiab] OR "1 year of age"[tiab] OR "age 2"[tiab] OR "age two"[tiab] OR "ages 2"[tiab] OR "ages two"[tiab] OR 2-year-old*[tiab] OR 2-years-old*[tiab] OR two-year-old*[tiab] OR two-years-old*[tiab] OR "2 years of age"[tiab] OR "age 3"[tiab] OR "age three"[tiab] OR "ages 3"[tiab] OR "ages three"[tiab] OR 3-year-old*[tiab] OR three-year-old*[tiab] OR 3-years-old*[tiab] OR three-years-old*[tiab] OR "3 years of age"[tiab] OR "age 4"[tiab] OR "age four"[tiab] OR "ages 4"[tiab] OR "ages four"[tiab] OR 4-year-old*[tiab] OR four-year-old*[tiab] OR 4-years-old*[tiab] OR four-years-old*[tiab] OR "4 years of age"[tiab] OR "age 5"[tiab] OR "age five"[tiab] OR "ages 5"[tiab] OR "ages five"[tiab] OR 5-year-old*[tiab] OR five-year-old*[tiab] OR 5-years-old*[tiab] OR five-years-old*[tiab] OR "5 years of age"[tiab] OR "age 6"[tiab] OR "age six"[tiab] OR "ages 6"[tiab] OR "ages six"[tiab] OR 6-year-old*[tiab] OR six-year-old*[tiab] OR 6-years-old*[tiab] OR six-years-old*[tiab] OR "6 years of age"[tiab] OR "age 7"[tiab] OR "age seven"[tiab] OR "ages 7"[tiab] OR "ages seven"[tiab] OR 7-year-old*[tiab] OR seven-year-old*[tiab] OR 7-years-old*[tiab] OR seven-years-old*[tiab] OR "7 years of age"[tiab] OR "age 8"[tiab] OR "age eight"[tiab] OR "ages 8"[tiab] OR "ages eight"[tiab] OR 8-year-old*[tiab] OR eight-year-old*[tiab] OR 8-years-old*[tiab] OR eight-years-old*[tiab] OR "8 years of age"[tiab] OR "age 9"[tiab] OR "age nine"[tiab] OR "ages 9"[tiab] OR "ages nine"[tiab] OR 9-year-old*[tiab] OR nine-year-old*[tiab] OR 9-years-old*[tiab] OR nine-years-old*[tiab] OR "9 years of age"[tiab] OR "age 10"[tiab] OR "age ten"[tiab] OR "ages 10"[tiab] OR "ages ten"[tiab] OR 10-year-old*[tiab] OR ten-year-old*[tiab] OR 10-years-old*[tiab] OR ten-years-old*[tiab] OR "10 years of age"[tiab] OR "age 12"[tiab] OR "age twelve"[tiab] OR "ages 12"[tiab] OR "ages twelve"[tiab] OR 12-year-old*[tiab] OR twelve-year-old*[tiab] OR 12-years-old*[tiab] OR twelve-years-old*[tiab] OR "12 years of age"[tiab] OR "age 14"[tiab] OR "age fourteen"[tiab] OR "ages 14"[tiab] OR "ages fourteen"[tiab] OR 14-year-old*[tiab] OR fourteen-year-old*[tiab] OR 14-years-old*[tiab] OR fourteen-years-old*[tiab] OR "14 years of age"[tiab]

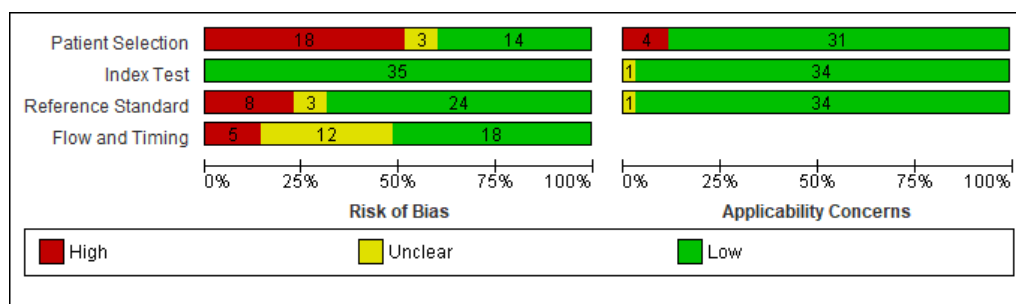
Concept 4: Outpatients, ambulatory care

"Ambulatory Care"[Mesh] OR "Ambulatory Care Facilities"[Mesh] OR "Office Visits"[Mesh] OR "Outpatient Clinics, Hospital"[Mesh] OR "General Practice"[Mesh] OR "Family Practice"[Mesh] OR "General Practitioners"[Mesh] OR "Physicians, Primary Care"[Mesh] OR "Physicians, Family"[Mesh] OR "Primary Health Care"[Mesh] OR "Emergency Medical Services"[Mesh] OR "Emergency Service, Hospital"[Mesh] OR "After-Hours Care"[Mesh] OR ambulatory[tiab] OR outpatient*[tiab] OR "primary health care"[tiab] OR "primary care"[tiab] OR "primary healthcare"[tiab] OR "prehospital care"[tiab] OR "after-hours"[tiab] OR "out-of-hours"[tiab] OR office-visit*[tiab] OR clinic-visit*[tiab] OR house-visit*[tiab] OR home-visit*[tiab] OR emergency-medical-service*[tiab] OR "emergency care"[tiab] OR "emergency healthcare"[tiab] OR emergency-service*[tiab] OR "urgent care"[tiab] OR "accident and emergency"[tiab] OR emergency-department*[tiab] OR emergency-unit*[tiab] OR emergency-ward*[tiab] OR health-center*[tiab] OR health-centre*[tiab] OR "polyclinic"[tiab] OR community-health-service*[tiab] OR "community health care"[tiab] OR "community healthcare"[tiab] OR community-health-facilit*[tiab] OR community-health-clinic*[tiab] OR walk-in-center*[tiab] OR walk-in-centre*[tiab] OR walk-in-clinic*[tiab] OR gp[tiab] OR general-practi*[tiab] OR general-physician*[tiab] OR general-doctor*[tiab] OR family-practi*[tiab] OR family-doctor*[tiab] OR family-physician*[tiab] OR emergency-doctor*[tiab] OR emergency-physician*[tiab] OR emergency-practitioner*[tiab]

Appendix 3. Risk of bias and applicability concerns summary



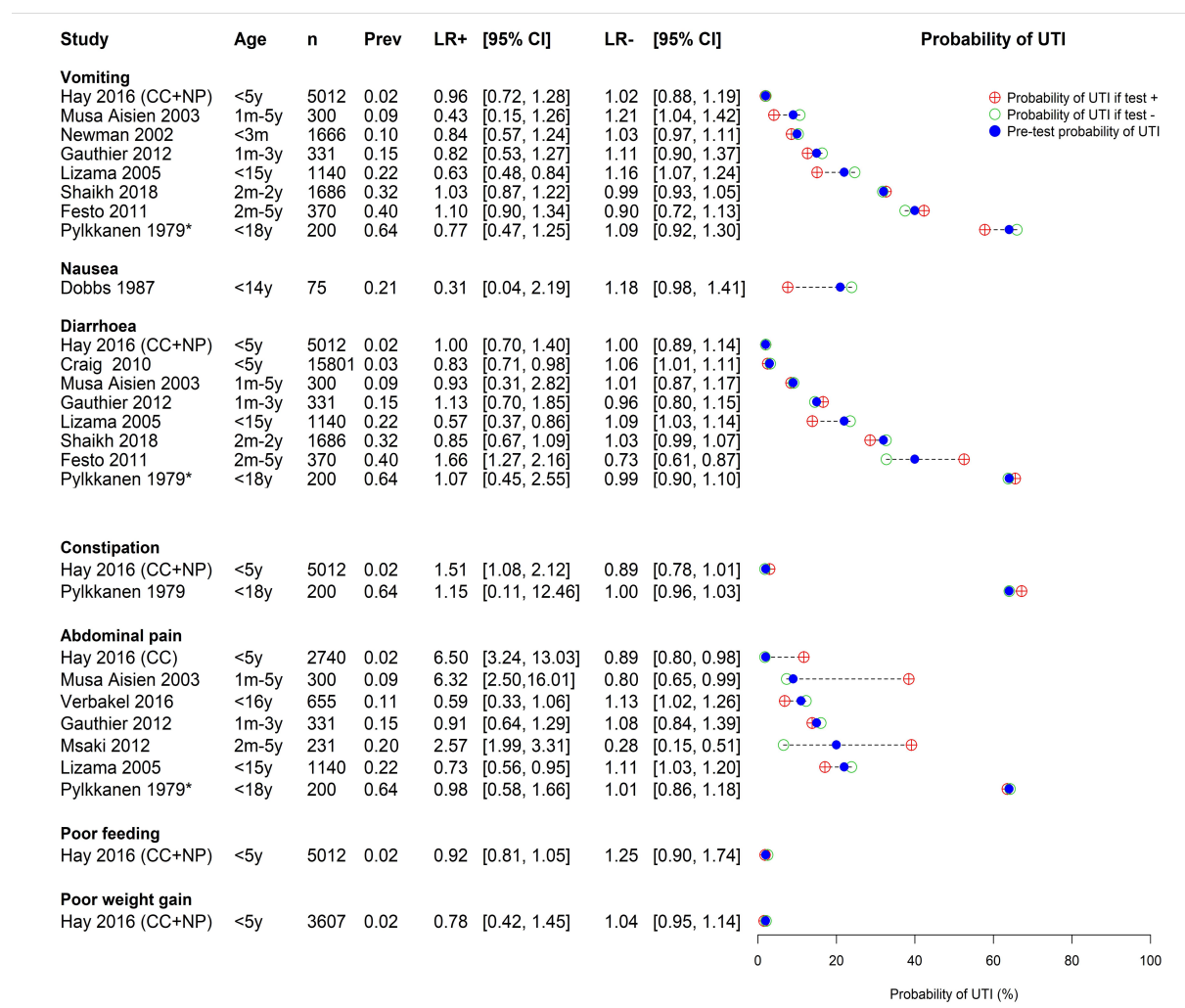
Review authors' judgements about each domain for each included study



Review authors' judgements about each domain presented as percentages across included studies

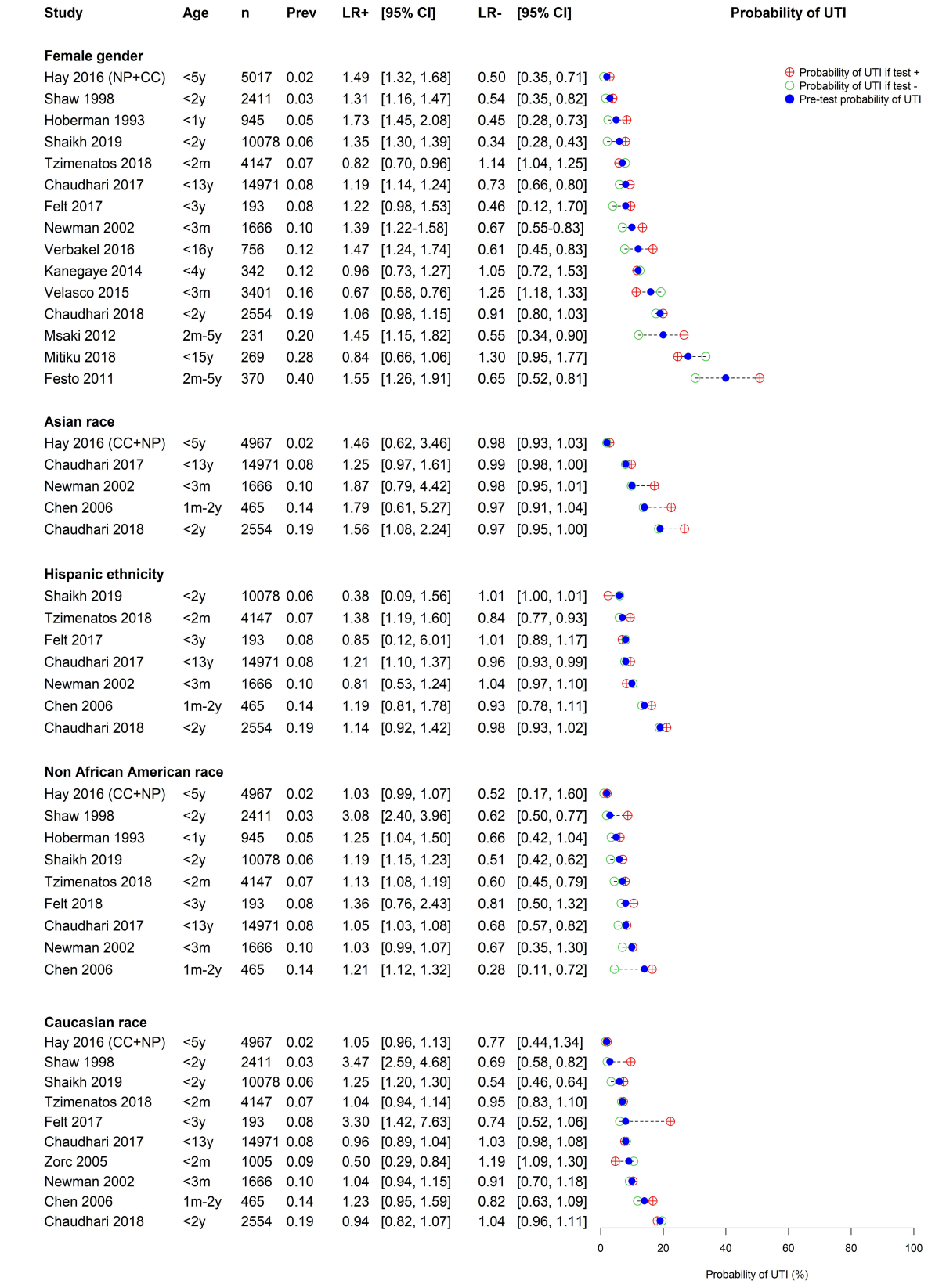
Appendix 4. Likelihood ratios and post-test disease probabilities (%) (dumbbell plots) of clinical features for urinary tract infections

(a) Abdominal features



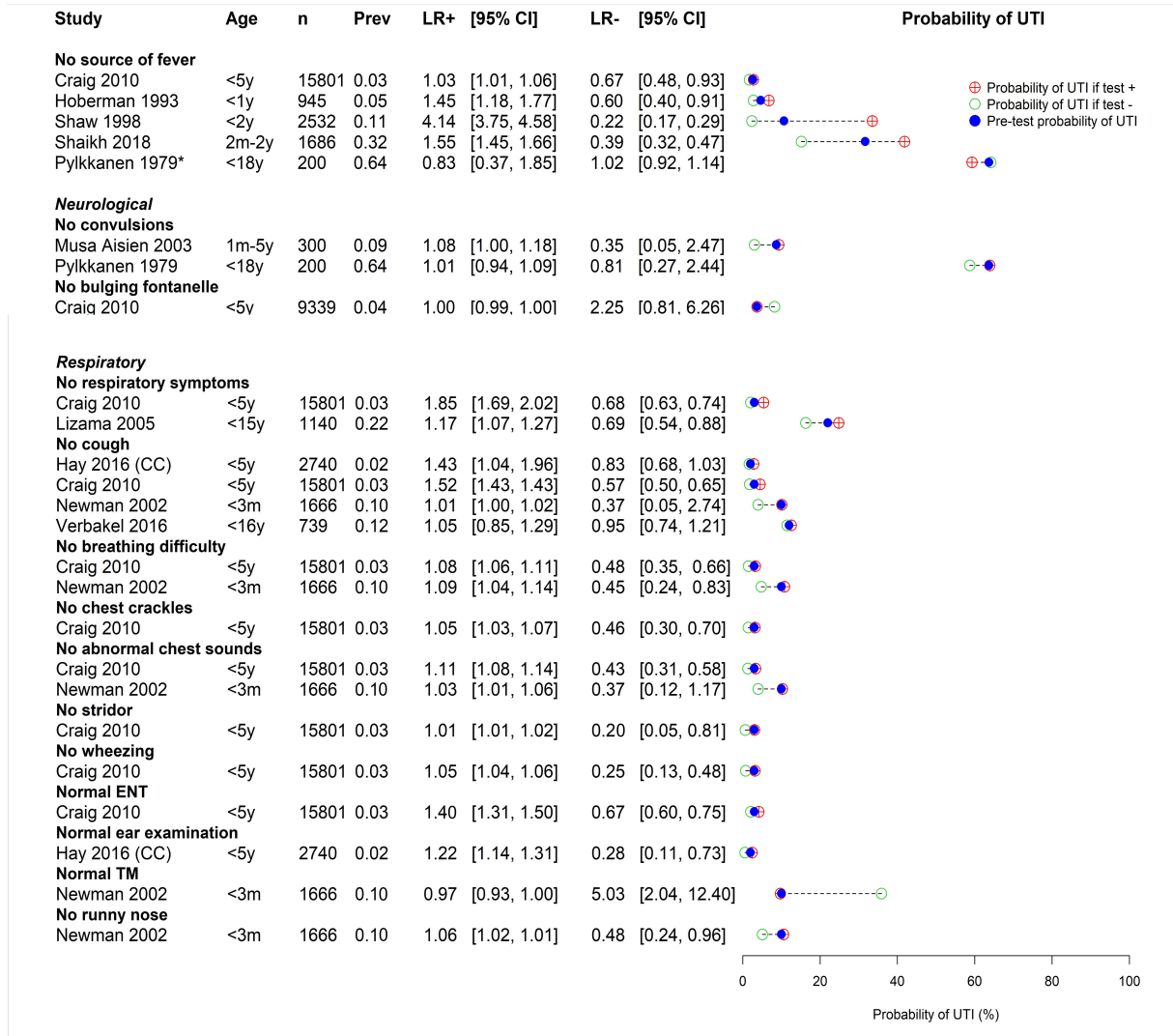
n=sample size; prev=prevalence; 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio; LR- =negative likelihood ratio; NP=nappy pad samples; CC=clean catch samples; *Data from Pylkkanen et al. (1979) were not included in the meta-analysis

(b) Ethnicity, race and gender for UTI



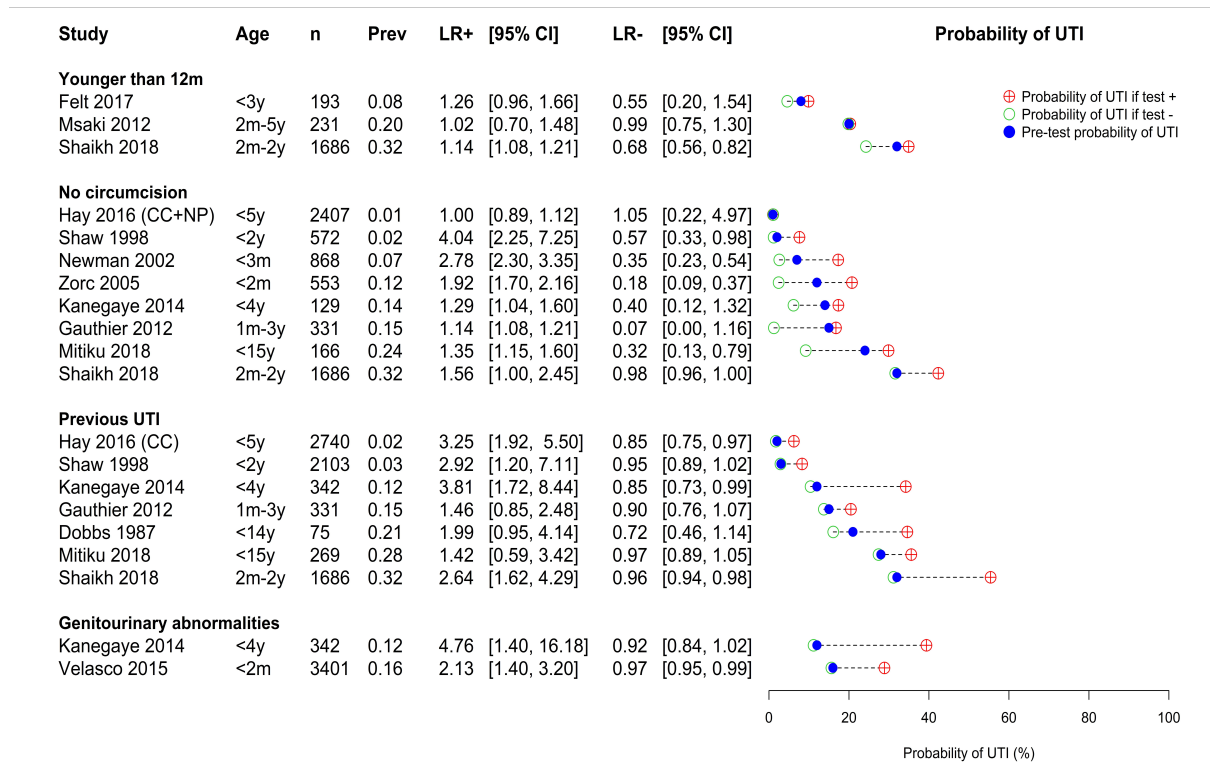
n=sample size, prev=prevalence, 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio, LR - =negative likelihood ratio, NP=nappy pad samples, CC=clean catch samples

(c) Absence of signs



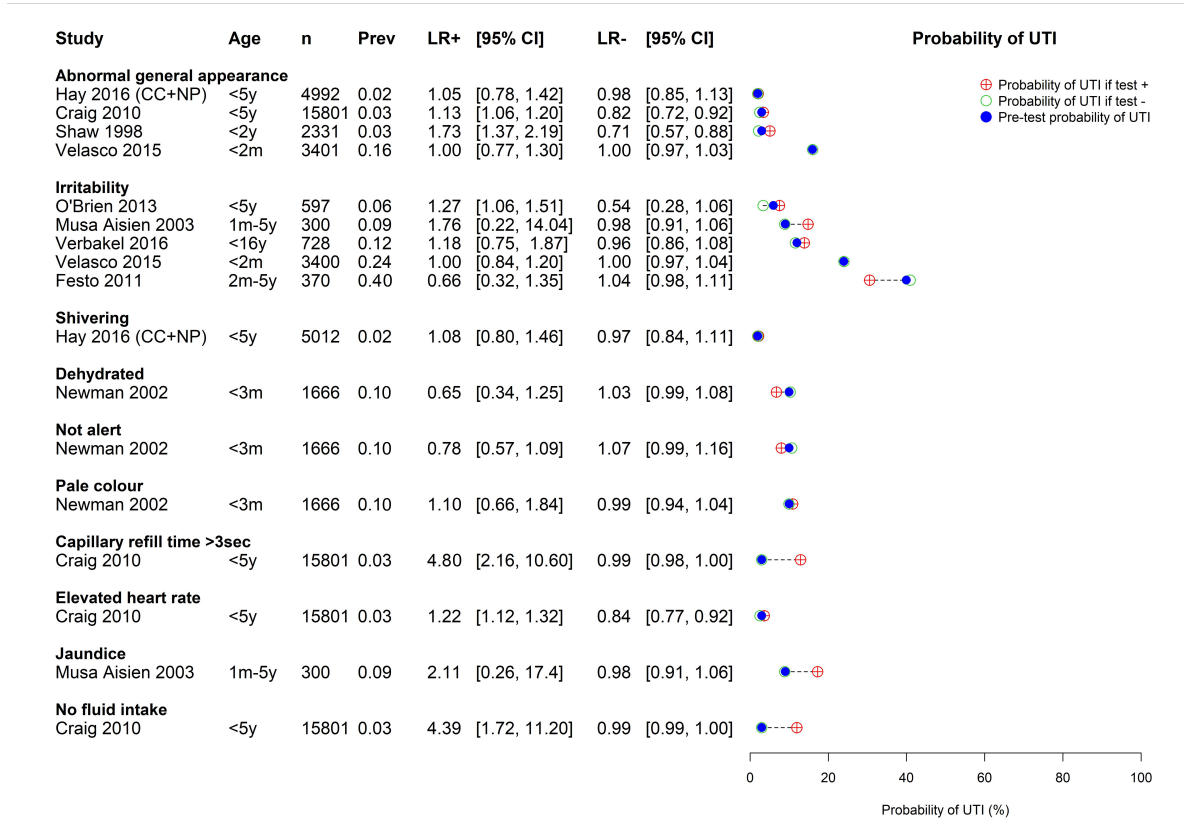
n=sample size; prev=prevalence; 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio; LR- =negative likelihood ratio; NP=nappy pad samples; CC=clean catch samples; *Data from Pylkkanen et al. (1979) were not included in the meta-analysis

(d) Medical history



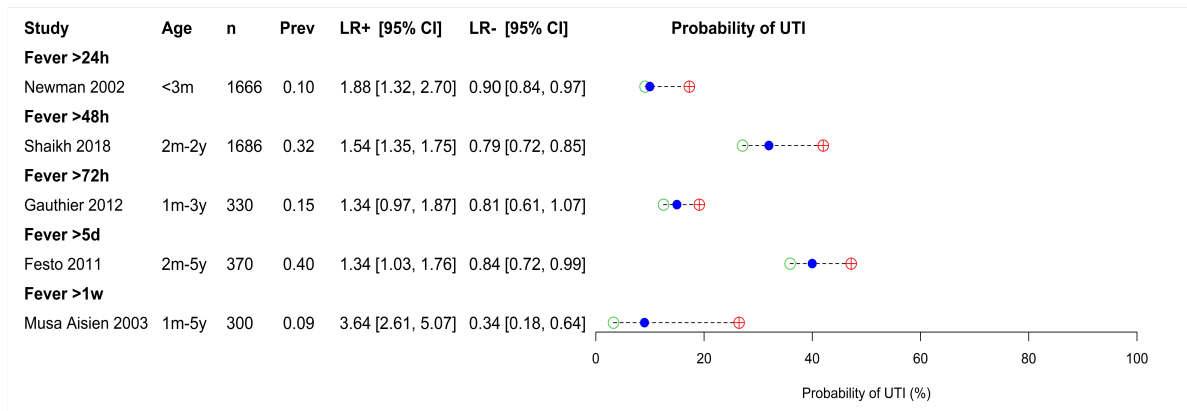
n=sample size, prev=prevalence, 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio, LR - =negative likelihood ratio, NP=nappy pad samples, CC=clean catch samples

(e) General appearance



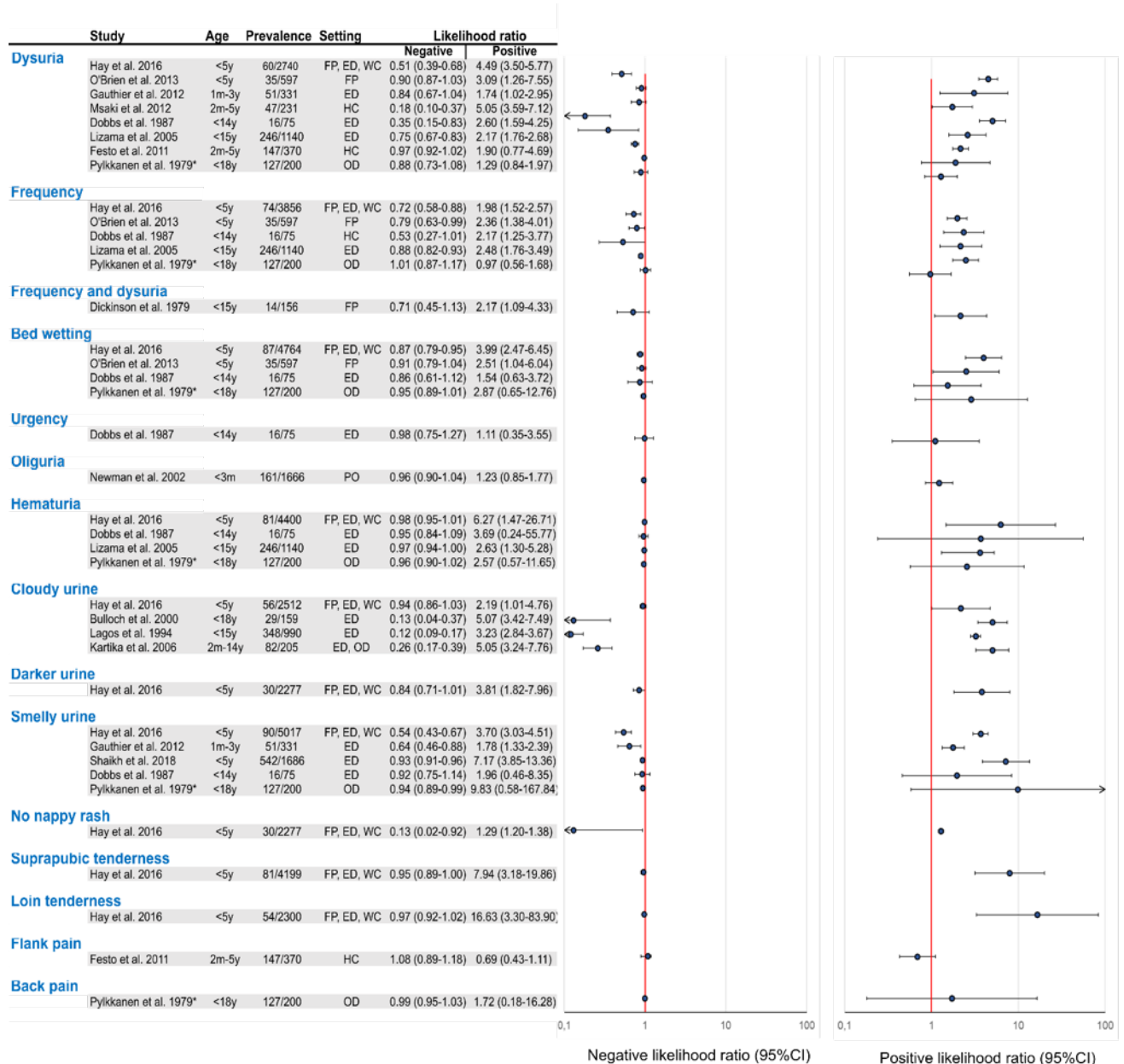
n=sample size, prev=prevalence, 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio, LR - =negative likelihood ratio, NP=nappy pad samples, CC=clean catch samples

(f) Fever duration



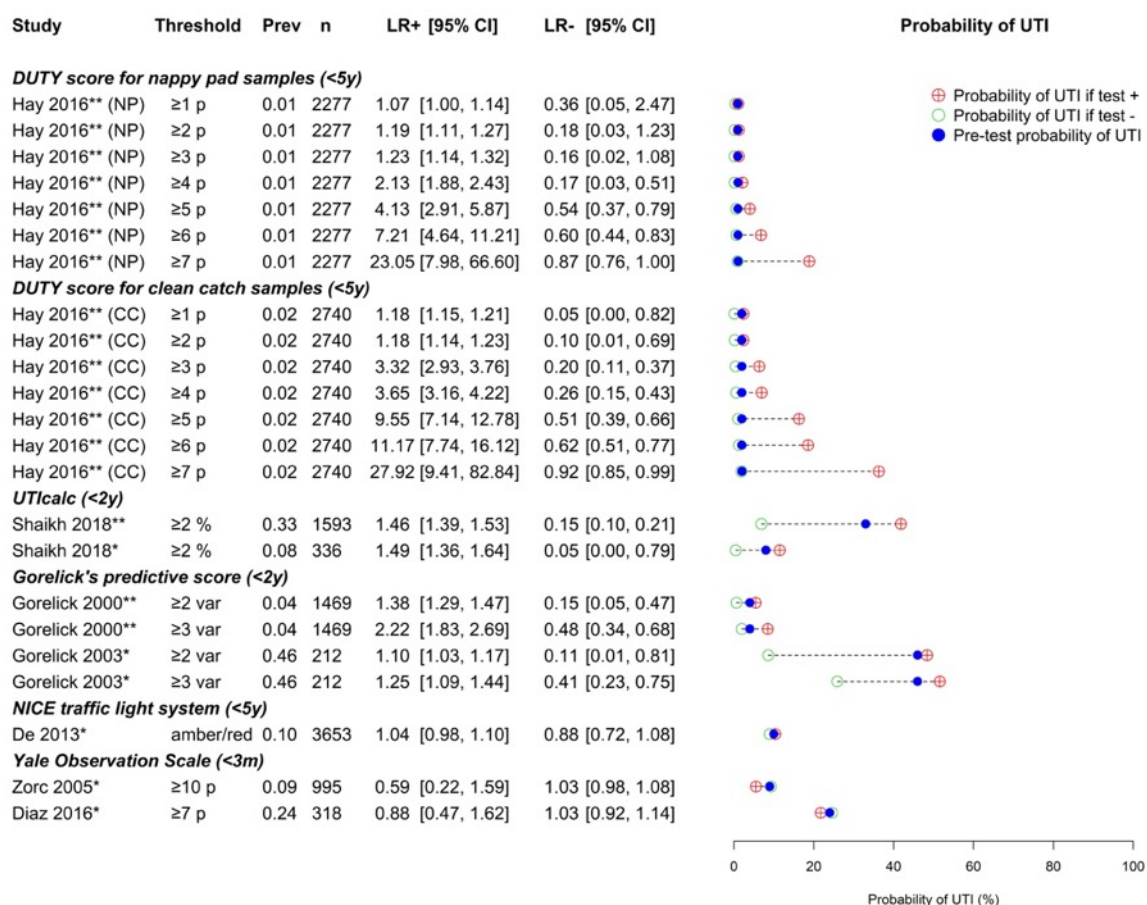
n=sample size, prev=prevalence, 95%CI=95% Confidence Interval; LR+ = positive likelihood ratio, LR - =negative likelihood ratio, NP=nappy pad samples, CC=clean catch samples

Appendix 5. Forest plots of likelihood ratios for urinary signs and symptoms



ED= emergency department, FP= family practice, WC= walk-in clinic, HC: health center, OD= outpatient department of a hospital, PO= pediatricians' office, *Data from Pylikkanen et al (1979) were not included in the meta-analyses

Appendix 6. Likelihood ratios and pre- and post-test disease probabilities (%) (dumbbell plots) of combinations of signs and symptoms for urinary tract infections



UTI= urinary tract infection; n= sample size; prev=prevalence; 95%CI: 95% Confidence Interval; LR+= positive likelihood ratio; LR-=negative likelihood ratio; NP= nappy pad; CC=clean catch; *=validation study; **=derivation study; YOS=Yale Observation Scale; NICE=National Institute for Health and Care Excellence; y=year; m=month

Appendix 7. Sensitivity analyses (summary estimates)

Clinical feature	No. studies *	n	Summary sensitivity (95% CI)	Summary specificity (95% CI)	Summary LR+ (95% CI)	Summary LR- (95% CI)
Red flags (LR+ \geq4) or features (LR- \leq0.25)						
Cloudy urine	4	3866	69% (30%-92%)	85% (72%-92%)	4.55 (3.73-5.56)	0.36 (0.13-1.02)
RS	3 (-1)	3661	67% (17-95%)	85% (68-94%)	4.47 (3.69-5.42)	0.40 (0.11-1.50)
Smelly urine	4	7109	31% (12%-59%)	93% (75%-98%)	4.13 (2.27-7.49)	0.75 (0.58-0.98)
ED only	3 (-1)	2092	23% (8-52%)	86% (86-99%)	5.47 (3.59-8.33)	0.81 (0.63-1.03)
Age <5y	3 (-1)	7034	43% (22-68%)	85% (69-94%)	2.90 (1.61-5.22)	0.67 (0.47-0.95)
RS	3 (-1)	7034	43% (22-68%)	85% (69-94%)	2.90 (1.61-5.22)	0.67 (0.47-0.95)
No circumcision	8	6712	88% (52%-98%)	52% (23%-80%)	1.81 (1.15-2.87)	0.24 (0.08-0.72)
ED only	5 (-3)	3271	88% (22-100%)	59% (16-91%)	2.12 (0.96-4.70)	0.21 (0.03-1.60)
UTI symptoms	6 (-2)	5291	80% (32-97%)	63% (29-87%)	2.13 (1.29-3.51)	0.33 (0.10-1.06)
Age <5y	7 (-1)	6546	89% (46%-99%)	54% (22%-84%)	1.95 (1.12-3.39)	0.20 (0.05-0.79)
Amber signs: LR+ \geq2 or LR- \leq0.5						
Dysuria	7	5413	40% (19%-66%)	88% (80%-93%)	3.28 (2.22-4.86)	0.68 (0.47-1.00)
ED only	3 (-5)	1475	29% (8-68%)	86% (67-95%)	2.13 (1.40-3.24)	0.82 (0.59-1.15)
other settings only	3 (-5)	1198	34% (17-56%)	90% (81-95%)	3.27 (2.07-5.18)	0.74 (0.57-0.96)
UTI symptoms	4 (-4)	4215	47% (13-83%)	86% (73-94%)	3.34 (1.90-5.88)	0.62 (0.30-1.27)
No UTI symptoms	3 (-5)	1198	34% (17-56%)	90% (81-95%)	3.27 (2.07-5.18)	0.74 (0.57-0.96)
Age <5y	5 (-2)	4198	34% (12%-67%)	91% (84%-95%)	3.59 (2.06-6.26)	0.73 (0.48-1.11)
RS	6 (-1)	5338	49% (27-72%)	86% (78-91%)	3.40 (2.32-4.97)	0.59 (0.38-0.91)
Frequency	4	5668	36% (22%-53%)	84% (74%-90%)	2.21 (1.78-2.75)	0.76 (0.65-0.90)
UTI symptoms	3 (-1)	5071	35% (17-59%)	86% (74-93%)	2.45 (1.77-3.41)	0.76 (0.59-0.97)
RS	3 (-1)	5593	44% (30-59%)	79% (71-86%)	2.11 (1.68-2.67)	0.71 (0.58-0.87)
Previous UTI	7	7546	15% (9%-24%)	94% (88%-97%)	2.31 (1.73-3.10)	0.91 (0.86-0.96)
ED only	4 (-3)	4462	14% (8-23%)	94% (88-97%)	2.25 (1.46-3.48)	0.92 (0.87-0.97)
Age <5y	5 (-2)	7202	13% (7%-21%)	95% (90%-97%)	2.51 (1.82-3.47)	0.92 (0.87-0.97)
RS	6 (-1)	7471	18% (11-28%)	93 (86-96%)	2.34 (1.63-3.34)	0.89 (0.83-0.95)
Signs with LR+<2 or LR- >0.5						
Diarrhea	7	24 640	20% (12%-30%)	78% (73%-83%)	0.91 (0.68-1.22)	1.03 (0.96-1.10)
ED only	5 (-2)	19 258	19% (9-35%)	77% (70-83%)	0.83 (0.51-1.33)	1.05 (0.95-1.16)
UTI symptoms	4 (-3)	8169	15% (8-27%)	80% (74-85%)	0.77 (0.53-1.12)	1.06 (1.00-1.12)
No UTI symptoms	3 (-4)	16 471	25% (13-44%)	76% (69-83%)	1.07 (0.71-1.60)	0.98 (0.85-1.13)
Age <5y	6 (-1)	23 500	22% (14-33%)	77% (72-81%)	0.96 (0.72-1.27)	1.01 (0.94-1.10)
Vomiting	7	10 505	27% (19%-38%)	69% (61%-76%)	0.89 (0.74-1.06)	1.05 (1.00-1.12)
ED only	4 (-3)	3457	27% (20-37%)	72% (63-79%)	0.97 (0.85-1.10)	1.01 (0.96-1.07)
UTI symptoms	4 (-3)	8169	27% (21-34%)	68% (63-73%)	0.85 (0.69-1.05)	1.07 (0.98-1.16)
No UTI symptoms	3 (-4)	2336	28% (12-51%)	70% (53-83%)	0.93 (0.70-1.24)	1.03 (0.93-1.14)
Age <5y	6 (-1)	9365	27% (17-38%)	70% (52-78%)	0.89 (0.72-1.09)	1.05 (0.98-1.12)
Abdominal pain	6	5397	29% (14%-51%)	84% (64%-94%)	1.86 (0.82-4.22)	0.84 (0.67-1.07)
ED only	3 (-3)	1771	25% (15-39)	81% (49-95%)	1.32 (0.47-3.72)	0.92 (0.72-1.78)
UTI symptoms	3 (-3)	4211	47% (19-77%)	65% (57-73%)	1.36 (0.67-2.77)	0.81 (0.44-1.50)
No UTI symptoms	3 (-3)	1186	16% (11-22%)	94% (80-98%)	2.61 (0.67-10.17)	0.90 (0.81-1.00)
Age <5y	4 (-2)	3602	37% (14%-67%)	88% (62%-97%)	3.18 (0.21-6.14)	0.71 (0.47-0.96)
RS	5 (-1)	4742	34% (15-58%)	78% (58-89%)	1.49 (0.68-3.25)	0.86 (0.62-1.20)
No cough	4	20 946	81% (33%-97%)	32% (7%-76%)	1.19 (0.93-1.52)	0.61 (0.34-1.07)
No UTI symptoms	3 (-1)	18 206	56% (41-70%)	59% (47-70%)	1.36 (1.10-1.70)	0.75 (0.58-0.96)
Age <5y	3 (-1)	20 207	88% (38-99%)	21% (3-72%)	1.12 (0.90-1.39)	0.55 (0.25-1.19)
RS	3 (-1)	20 207	88% (38-99%)	21% (3-72%)	1.12 (0.90-1.39)	0.55 (0.25-1.19)

Irritability	5	5395	15% (4%-48%)	85% (63%-95%)	1.00 (0.67-1.48)	1.00 (0.93-1.07)
Age <5y	4 (-1)	4667	14% (2%-56%)	85% (56%-96%)	0.97 (0.49-1.45)	1.01 (0.93-1.08)
RS	4 (-1)	4667	9% (3-21%)	91% (81-96%)	0.91 (0.55-1.48)	1.01 (0.97-1.06)
Abnormal appearance	4	26 525	36% (17%-60%)	70% (50%-85%)	1.21 (1.02-1.44)	0.91 (0.80-1.04)
ED only	3 (-1)	21 533	33% (12-65%)	70% (43-88%)	1.11 (0.98-1.26)	0.95 (0.86-1.06)
Female gender	15	47 351	66% (57%-74%)	47% (42%-52%)	1.24 (1.11-1.39)	0.73 (0.58-0.91)
ED only	9 (-6)	39 042	62% (48-75%)	47% (41-54%)	1.18 (0.99-1.40)	0.80 (0.60-1.08)
other settings only	4 (-11)	2536	72% (59-83%)	47% (37-57%)	1.37 (1.20-1.56)	0.59 (0.43-0.81)
UTI symptoms	9 (-6)	13 436	65% (54-74%)	47% (41-53%)	1.22 (1.04-1.42)	0.76 (0.58 (0.98)
No UTI symptoms	6 (-9)	6424	70% (50-85%)	47% (40-54%)	1.32 (1.12-1.55)	0.64 (0.40-0.02)
Age <5y	12 (-2)	43 772	66% (64-76%)	45% (40-50%)	1.19 (1.05-1.35)	0.77 (0.59-1.00)
RS	13 (-2)	31 624	66% (55-75%)	46% (41-51%)	1.21 (1.07-1.36)	0.75 (0.59-0.96)
Caucasian	10	42 456	50% (34%-65%)	58% (42%-73%)	1.18 (0.96-1.46)	0.87 (0.73-1.04)
ED only	8 (-2)	35 824	56% (37% -74%)	52% (33-70%)	1.16 (0.93-1.44)	0.85 (0.66-1.09)
UTI symptoms	8 (-2)	39 786	50% (32-67%)	55% (37-72%)	1.10 (0.88-1.38)	0.92 (0.75-1.13)
Age <5y	9 (-1)	27 486	53% (35-71%)	57% (37-74%)	1.23 (0.95-1.59)	0.82 (0.66-1.03)
RS	9 (-1)	27 486	63% (35-71%)	57% (37-74%)	1.23 (0.96-1.59)	0.82 (0.66-1.03)
Hispanic ethnicity	7	34 074	12% (4%-32%)	89% (76%-95%)	1.03 (0.74-1.44)	1.00 (0.95-1.05)
ED only	6 (-1)	32 408	13% (3-38%)	88% (72-95%)	1.06 (0.74-1.51)	0.99 (0.93-1.05)
UTI symptoms	6 (-1)	32 408	13% (3-38%)	88% (72-95%)	1.06 (0.74-1.51)	0.99 (0.93-1.05)
Age <5y	6 (-1)	19 103	11% (3-35%)	89% (74-96%)	1.01 (0.68-1.51)	1.00 (0.95-1.05)
RS	6 (-1)	19 103	11% (3-35%)	89% (74-96%)	1.01 (0.68-1.51)	1.00 (0.95-1.05)
Asian race	5	24 623	5% (4%-7%)	96% (95%-97%)	1.42 (1.09-1.86)	0.98 (0.97-1.00)
ED only	3 (-2)	17 990	7% (5-9%)	97% (95-98%)	2.02 (1.19-3.41)	0.97 (0.94-0.99)
UTI symptoms	4 (-1)	22 957	5% (4-7%)	96% (95-97%)	1.44 (1.07-1.93)	0.98 (0.97-1.00)
Age <5y	4 (-1)	9652	5% (4-7%)	97% (96-98%)	1.45 (1.01-2.06)	0.98 (0.97-1.00)
RS	4 (-1)	9652	5% (4-7%)	97% (96-98%)	1.45 (1.01-2.06)	0.98 (0.97-1.00)
Non-African American	10	42 397	85% (76%-91%)	27% (14%-45%)	1.17 (1.02-1.33)	0.55 (0.48-0.63)
ED only	8 (-2)	35 764	88% (79-93%)	22% (10-40%)	1.12 (1.00-1.26)	0.56 (0.47-0.68)
UTI symptoms	8 (-2)	39 786	86% (75-93%)	26% (12-48%)	1.16-0.99-1.36)	0.54 (0.46-0.65)
Age <5y	9 (-1)	27 426	84% (74-91%)	29% (15-49%)	1.18-1.01-1.38)	0.55 (0.48-0.64)
RS	9 (-1)	27 426	84% (74-91%)	29% (15-49%)	1.18-1.01-1.38)	0.55 (0.48-0.64)

Bivariate random effects model by Chu and Cole et al. (2006); UTI= urinary tract infection; No. = Number; n= sample size; LR+ = positive likelihood ratio; LR-= negative likelihood ratio; y=years; ED only= analysis of studies performed at the emergency department; other settings only= analysis of studies performed at outpatient settings, other than the ED; UTI symptoms= analysis of studies that included children with UTI symptoms; no UTI symptoms= analysis of studies that included children with fever or acute illness episode, regardless of UTI symptoms; RS= analysis of studies with suboptimal reference standard test not included; 95%CI = 95% confidence intervals

*Meta-analysis not possible if <3 studies available per subgroup

Supplemental Table 1. Characteristics of Included Studies

Study	Setting, Country	Design	Age range, (median/mean ^a) No. girls (%)	Prevalence ^b (%)	Inclusion criteria	Reference standard
Bonadio et al. 1991 ⁴⁴	ED USA	Retrospective, cons	1-2m (NR) NR	16/683 (2.3%)	Fever (>38°C)	Urine culture single pathogen ≥ 10 ⁵ cfu/ml (NR)
Bulloch et al. 2000 ²³	ED USA	Prospective, conv, cx	1m-19y (5.8y) 122/159 (77%)	29/159 (18.2%)	Specimen available	Urine culture ≥10 ⁴ cfu/ml (UC, ≥10 ⁵ cfu/ml (MS,UC)
Craig et al. 2010 ⁴³	ED Australia	Prospective, cons, cx	<5y (NR) 8814/15 781 (56%)	543/15 781(3.4%)	Fever (≥38.0°C) or 'felt hot'	Urine culture any cfu/ml(SPA), ≥10 ⁴ cfu/ml (UC), ≥10 ⁵ cfu/ml (MS)
Chaudhari et al. 2017 ⁴⁷	ED USA	Retrospective, cx	<13y (1.5y) NR (60%)	1150/14 971(7.7%)	Test results available	Urine culture single pathogen ≥5x10 ⁴ cfu/ml (UC), ≥5x10 ⁴ cfu/ml (boys) (MS), ≥10 ⁵ cfu/ml (girls) (MS)
Chaudhari et al. 2018 ²⁴	ED USA	Retrospective, cons, cx	<2y (6.1m) 1542/2554 (60%)	494/2554 (19.3%)	Test results available	Urine culture single pathogen ≥5x10 ⁴ cfu/ml (UC)
Chen et al. 2006 ²⁵	ED USA	Retrospective	1m-2y (NR) NR (57%)	64/465 (13.8%)	Fever (>37.9°C) and specimen available	Urine culture ≥10 ³ cfu/ml (SPA), ≥10 ⁴ cfu/ml (UC), ≥10 ⁵ cfu/ml (BS)
De et al. 2013 ⁵³	ED Australia	Prospective, cons, cx	<5y (NR) NR	362/3653 (9.9%)	Fever (≥38.0°C) or 'felt hot'	Urine culture any cfu/ml (SPA), ≥10 ⁴ cfu/ml (UC), ≥10 ⁵ cfu/ml (CC, MS)
Diaz et al. 2016 ⁵²	ED Spain	Retrospective	<3m (43.4d) 128/318 (40%)	76/318 (23.9%)	Fever (≥38°C) and tests results available	Urine culture ≥5x10 ⁴ cfu/ml (SPA, UC)

Dickinson et al. 1979 ⁴⁸	FP UK	Prosp, cx	<15y (NR) NR (67%)	14/156 (9.0%)	Symptoms of UTI	Urine culture single pathogen $\geq 10^5$ cfu/ml in three consecutive specimens (MS, BS)
Dobbs et al. 1987 ²⁶	HC UK	Prosp, cx	0-14y (NR) NR	16/75 (21.3%)	Symptoms of UTI	Urine culture $\geq 10^5$ cfu/ml, $\geq 10^4$ to 10^5 cfu/ml and $\geq 10^2$ wbc/mm ³ (MS)
Duong et al. 2016 ⁴⁹	ED Belgium	Prosp, cons, cx	≤ 16 y (44m) 739/1247 (59%)	221/1247 (17.7%)	Specimen available	Urine culture single pathogen Any cfu/ml (SPA), $\geq 10^5$ cfu/ml (CC, UC)
Felt et al. 2017 ²⁷	ED, USA	Prosp, conv, cx	<3y (9m) 139/193 (72%)	15/193 (7.8%)	Fever ($\geq 38^\circ\text{C}$) and specimen available	Urine culture any cfu/ml (UC or SPA)
Festo et al. 2011 ²⁸	HC, Tanzania	Prosp, cons, cx	2m-5y (18m) 176/370 (48%)	147/370 (39.7%)	Fever	Urine culture any cfu/ml (SPA), $\geq 10^5$ cfu/ml (MS)
Gauthier et al. 2012 ⁴⁶	ED Canada	Prosp, cons, cx	1m-3y (12m) 189/331 (57%)	51/331 (15.4%)	Symptoms of UTI: FWS ($>38.5^\circ\text{C}$), irritability or vomiting	Urine culture any cfu/ml of gram negative species (SPA), $\geq 10^4$ cfu/ml gram positive species (SPA), $\geq 10^5$ cfu/ml (UC), $\geq 10^4$ cfu/ml pseudomonas species (UC), $\geq 10^5$ cfu/ml (CC or MS)
Gorelick et al. 2000 ⁵⁰	ED USA	Prosp, cons, cx der	<2y (11 m) ^a 1469/1469 (100%)	63/1469 (4.3%)	FWS ($\geq 38.3^\circ\text{C}$) in girls	Urine culture single specimen $\geq 10^4$ cfu/ml (UC)
Gorelick et al. 2003 ⁵¹	ED USA	Retrospective, ncc	1m-2y (9.4m) ^a 212/212 (100%)	98/212 (46.2%)	Test results available	Urine culture pathogen $\geq 5 \times 10^4$ cfu/ml (UC)
Hay et al. 2016 ¹⁵	FP,ED,WC UK	Prosp, cons, cx	<5y (CC: 94% >2y) (NP: 82% <2y) CC:1473/2740 (54%)	CC:60/2740 (2.2%) NP:30/227 7 (1.3%)	≥ 1 symptoms of UTI (NICE-2)	Urine culture single pathogen $\geq 10^5$ cfu/ml (NP, CC, BS), or pathogen $\geq 10^5$ cfu/ml with 1000-fold difference between the growth of this and the next species (NP, CC, BS)

			NP:1094/2277 (48%)			
Hoberman et al. 1993²⁹	ED USA	Prosp, cons, cx	≤1y (68% >2m) 419/945 (44%)	50/945 (5.3%)	Fever (≥38.3°C)	Urine culture ≥10 ⁴ cfu/ml (UC)
Kanegaye et al. 2014³⁰	ED USA	Prosp, conv, cx	≤4y (8.1m) 202/342 (59%)	42/342 (12.3%)	Fever (≥38°C) and test results available	Urine culture ≥5x10 ⁴ cfu/ml (UC)
Kartika et al. 2006³¹	ED,OD Indonesia	Prosp, cx	2m-14y (5.6y) 118/342 (58%)	82/205 (40.0%)	Suspicion of UTI	Urine culture single pathogen (CC, MS)
Lagos et al. 1994³²	ED Chile	Prosp, cx	<15y (26% <2y) (59% <5y) 737/990 (74%)	348/990 (35.2%)	Suspicion of UTI	Urine culture ≥10 ⁵ cfu/ml and ≥10wbc/mm ³ (SPA, MS or BS) or 2 positive cultures obtained within 5d
Lizama et al. 2005³³	ED Chile	Retrosop, cons	11d-14y (2.3y) 739/1140 (65%)	246/1140 (21.6%)	Specimen available	Urine culture any cfu/ml (SPA) ≥10 ⁴ cfu/ml (UC), ≥10 ⁵ cfu/ml (MS)
Mitiku et al. 2018³⁴	OD Ethiopia	Prosp, cons, cx	<15y (20.5%<1y) (60% <5y) 103/269 (38%)	74/269 (27.5%)	Symptoms of UTI: ≥1: t°≥37.5°C, vomiting, dysuria, frequency, urgency, loin pain, darker change	Urine culture ≥10 ⁵ cfu/ml (MS)
Msaki et al. 2012³⁵	HC Tanzania	Prosp, cons, cx	2m-5y (15m) 126/231 (55%)	47/231 20.3%	Fever (≥37.5°C)	Urine culture any cfu/ml (SPA), ≥10 ⁵ cfu/ml (MS)

Musa-Aisien et al. 2003 ³⁶	ED Nigeria	Prosp, cons, cx	1m-5y (18m) 123/300 (41%)	26/300 (8.7%)	Fever ($\geq 38^{\circ}\text{C}$)	Urine culture $\geq 10^5$ cfu/ml (SPA, CC or MS)
Newman et al. 2002 ³⁷	PO USA	Prosp, cx	$\leq 3\text{m}$ (32% <1m) (75% <2m) 798/1666 (48%)	161/1666 9.7%	Fever ($\geq 38^{\circ}\text{C}$)	Urine culture single pathogen $\geq 10^2$ cfu/ml (SPA), $\geq 2 \times 10^4$ cfu/ml (UC), $\geq 10^5$ cfu/ml (BS, CC)
O'Brien et al. 2013 ⁴	FP UK	Prosp, cons, cx	$\leq 5\text{y}$ (2.3y) 284/597 (48%)	35/597 (5.9%)	Illness episode <28d	Urine culture $\geq 10^5$ cfu/ml (NP, CC)
Pylkkanen et al. 1979 ³⁸	OD Finland	Prosp, cx	<18y (64.5% $\leq 2\text{y}$) NR	127/200 (63.5%)	Suspicion of UTI	Urine culture any cfu/ml (Uricult and blood agar plate; SPA)
Shaikh et al. 2018 ¹⁶	ED USA	Retrosp, ncc	2m-2y (72.9% <1y) der: 1216/1686 (72%) val: 291/384 (76%)	der: 542/1686 (32.2%) val: 30/384 (7.8%)	Fever ($\geq 38^{\circ}\text{C}$) and specimen available cases=positive culture controls=negative culture	Urine culture $\geq 5 \times 10^4$ cfu/ml (UC) and pyuria
Shaikh et al. 2019 ⁴⁵	ED USA	Retrosp, cons, cx	<2y (7.0m) 6743/10 078 (67%)	617/10 078 (6.1%)	Test results available	Urine culture pathogen $\geq 5 \times 10^4$ cfu/ml (UC)
Shaw et al. 1998 ³⁹	ED USA	Prosp, cons, cx	boys <1y (41.5% <6m) girls <2y (55.3% <12m) 1469/2411 (61%)	80/2411 (3.3%)	Fever ($\geq 38.5^{\circ}\text{C}$) and symptoms of UTI	Urine culture $\geq 10^4$ cfu/ml (UC)

Tzimenatos et al. 2018 ⁴⁰	ED USA	Prosp, conv, cx	<60d (31.3%<28d) 1771/4147 (43%)	289/4147 (7.0%)	Fever (>38°C) and test results available	Urine culture pathogen ≥10 ³ cfu/ml (SPA), ≥5x10 ⁴ cfu/ml (UC)
Velasco et al. 2015 ¹⁷	ED Spain	Prosp, cons, cx	<90d (46d) 1372/3401 (40%)	547/3401 (16.1%)	Fever (≥38°C) and test results available	Urine culture single pathogen ≥5x10 ⁴ cfu/ml (SPA, UC)
Verbakel et al. 2015 ⁴¹	FP, ED,OD Belgium	Prosp, cons, cx	1m-16y (2.0y) 362/756 (48%)	87/756 (11.5%)	Illness episode ≤5d	Urine culture ≥10 ⁵ cfu/ml (NR)
Zorc et al. 2005 ⁴²	ED USA	Prosp, cx	≤60d (35.5d) ^a 439/1005 (44%)	91/1005 (9.1%)	Fever (≥38°C)	Urine culture ≥10 ³ cfu/ml(SPA), ≥5x10 ⁴ cfu/ml (UC), ≥10 ⁴ cfu/ml + positive urinalysis (UC)

UTI= urinary tract infection; USA= United States; UK= United Kingdom; ED= Emergency departments; FP= family practices; OD= outpatient department of a hospital; HC= health centers; PO= pediatricians' offices; Prosp= Prospective design; retrosp= Retrospective design; cx= Cross-sectional design; cons= Consecutive enrolment; conv= convenience sampling; ncc= nested case-control; y= years; d= days; m= months; °C= degrees Celsius; FWS = fever without a source for infection; CRP= C-reactive protein; WBC= white blood cell (in urine); UC= urethral catheterization; SPA=suprapubic aspiration; MS=midstream sample; CC= clean catch sample (first stream); BS=bag specimen; NP= nappy pad sample; NR= not reported; POC=point-of-care; hpf = high polarized field; cfu= colony forming unit; ml=milliliter

^amean (median not provided); ^bprevalence= No. of children with UTI/sample size

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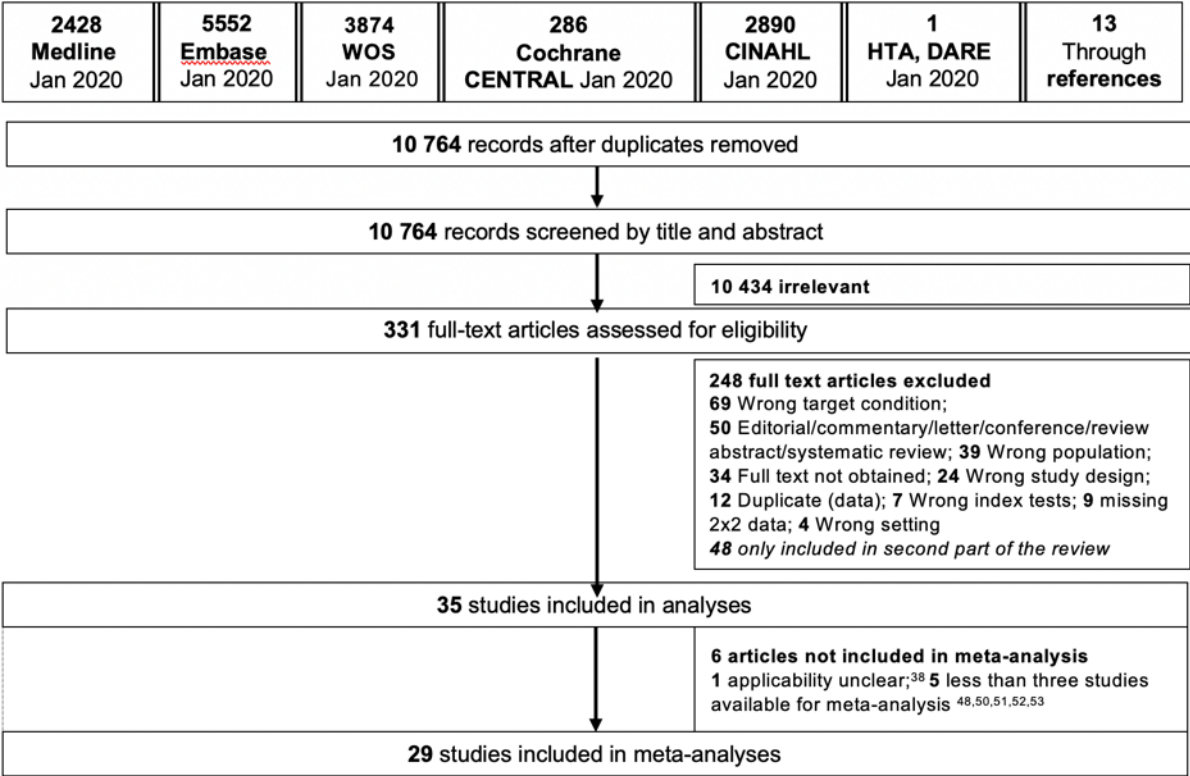
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Supplemental Figure 1. PRISMA flow diagram of included studies



Legend: PRISMA = Preferred Reporting Items for a Systematic review and Meta-Analysis of Diagnostic Test Accuracy Studies; WOS = Web Of Science; HTA = Health Technology Assessments